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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 530

[Docket No. 01N–0499]

Topical Nitrofurans; Extralabel Animal Drug Use; Order of Prohibition

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (we) is issuing an order prohibiting the extralabel use of topical nitrofuran animal and human drugs in food-producing animals. We are issuing this order based on evidence that extralabel use of topical nitrofuran drugs in food-producing animals may result in the presence of residues that we have determined to be carcinogenic and to not have been shown to be safe. We find that such extralabel use "presents a risk to the public health" for the purposes of the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA).

DATES: This rule is effective [*insert date 90 days after date of publication in the* **Federal Register**]. We invite your written or electronic comments. We will consider all comments that we receive by [*insert date 60 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit your written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

FOR FURTHER INFORMATION CONTACT: Gloria J. Dunnavan, Center for Veterinary Medicine (HFV–6), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–1726, e-mail: gdunnava@cvm.fda.gov.

SUPPLEMENTARY INFORMATION:

cv9865

NFR-1

I. AMDUCA

AMDUCA (Public Law 103–396) was signed into law on October 22, 1994. It amended the Federal Food, Drug, and Cosmetic Act (the act) to permit licensed veterinarians to prescribe extralabel uses of approved animal and human drugs in animals. However, section 512(a)(4)(D) of the act (21 U.S.C. 360b(a)(4)(D)) gives us authority to prohibit an extralabel drug use in animals if, after affording an opportunity for public comment, we find that such use presents a risk to the public health.

We published the implementing regulations (codified at part 530 (21 CFR part 530)) for AMDUCA in the **Federal Register** of November 7, 1996 (61 FR 57732). The sections regarding prohibition of extralabel use of drugs in food-producing animals are found at §§ 530.21 and 530.25. These sections describe the basis for issuing an order prohibiting an extralabel drug use in food-producing animals and the procedure to be followed in issuing an order of prohibition. We may issue a prohibition order if we find that extralabel use in animals presents a risk to the public health. Under § 530.3(e), this means that we have evidence that demonstrates that the use of the drug has caused or likely will cause an adverse event.

Section 530.25 provides for a public comment period of not less than 60 days. It also provides that the order of prohibition will become effective 90 days after the date of publication, unless we revoke the order, modify it, or extend the period of public comment. The list of drugs prohibited from extralabel use is found in § 530.41. The current list of drugs prohibited from extralabel use in food-producing animals includes furazolidone and nitrofurazone, but it contains the parenthetical statement "(except for approved topical use)".

II. Nitrofurans

In 1991, and after a full evidentiary hearing, we withdrew the approvals for furazolidone and nitrofuranzone labeled for antiprotozoal use in a wide variety of conditions in poultry and swine. (See the **Federal Register** of August 23, 1991 (56 FR 41902).) These withdrawals were based on our determination that use of the drugs resulted in residues in edible tissues for human

food and that residues of these drugs were not shown to be safe, in part because both drugs are carcinogenic. We did not, however, withdraw the approvals of these products for use in nonfood animals or for topical use in food-producing animals. Moreover, while our current regulations in § 530.41 prohibit extralabel use of approved furazolidone and nitrofurazone products in food-producing animals, this prohibition does not extend to topical use in food-producing animals. These topical uses in food-producing animals were allowed because there was no evidence that such use of furazolidone and nitrofuranzone resulted in residues in edible tissues.

However, a recent carbon-14 (C–14) radio-label residue depletion study that we conducted showed that detectable levels of nitrofuran derivatives are present in edible tissues (milk, meat, kidney, liver) of cattle treated by the ocular (eye) route (Ref. 1). This study, coupled with our findings in our prior withdrawal action, means that residues, which are carcinogenic and have not been shown to be safe, will likely be present at slaughter as a result of topical uses of nitrofurans, including furazolidone and nitrofurazone, in food-producing animals.

We advised all manufacturers of nitrofuran drugs that were approved for ocular use in food-producing animals of the evidence and the manufacturers revised their labels to remove those indications. (See, for example, 65 FR 41587 (July 6, 2000).) Some lot numbers of these drugs may remain in commercial distribution channels with the former labels that contain indications for food-producing animals. These products, however, are not approved for use in food-producing animals and, therefore, are adulterated and misbranded. Some topical and ophthalmic nitrofuran products are still approved for certain uses in nonfood animals. Under the current regulations governing extralabel use, these remaining approved topical and ophthalmic products are not prohibited from extralabel topical use in food-producing animals. However, as stated previously, there is evidence that these uses will result in residues in edible tissues. Because of the likelihood of this adverse event, by this order of prohibition, we are prohibiting all extralabel uses, including extralabel topical use, in food-producing animals of nitrofuran products that are approved for use

in nonfood animals or humans. Therefore, no nitrofuran product may be legally used in food-producing animals.

III. Request for Comments

We are providing 60 days from the date of this publication for you to comment. The order will become effective [*insert date 90 days after date of publication in the* **Federal Register**], unless we revoke or modify the order or extend the comment period. You may submit written or electronic comments to the Dockets Management Branch (address above) by [*insert date 60 days after date of publication in the* **Federal Register**]. Please identify your comments with the docket number found in brackets in the heading of this document. You may read any comments that we receive at our Dockets Management Branch reading room (address above). The reading room is open from 9 a.m. to 4 p.m., Monday through Friday, except for Federal holidays.

IV. Order of Prohibition

Therefore, I hereby issue the following order under section 512(a)(4)(D) of the act and 21 CFR 530.21 and 530.25. We find that extralabel use of nitrofurans in food-producing animals likely will cause an adverse event, which constitutes a finding under section 512(a)(4)(D) of the act that extralabel use of these drugs in food-producing animals presents a risk to the public health. Therefore, we are prohibiting all extralabel uses of these drugs in food-producing animals.

V. Reference

The following information has been placed on display in the Dockets Management Branch (address above). You may view it between 9 a.m. and 4 p.m., Monday through Friday.

1. Smith, D. J., G. D. Paulson, and G. L. Larsen, "Distribution of Radiocarbon After Intermammary, Intrauterine or Ocular Treatment of Lactating Cows With Carbon-14 Nitrofurazone," *Journal of Dairy Science*, vol. 81, pp. 979–988, 1998.

List of Subjects in 21 CFR Part 530

Administrative practice and procedure, Advertising, Animal drugs, Labeling, Reporting and recordkeeping requirements.

Accordingly, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Director of the Center for Veterinary Medicine, 21 CFR part 530 is amended as follows:

PART 530—EXTRALABEL DRUG USE IN ANIMALS

1. The authority citation for 21 CFR part 530 continues to read as follows:

Authority: 15 U.S.C. 1453, 1454, 1455; 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 360b, 371, 379e.

§ 530.41 [Amended]

2. Section 530.41 *Drugs prohibited for extralabel use in animals* is amended in paragraphs (a)(7) and (a)(8) by removing the parenthetical phrase "(except for approved topical use)".

Dated: 11/9/01
November 9, 2001.

Stephen F. Sundlof,
Director,
Center for Veterinary Medicine.

[FR Doc. 01–????? Filed ??–??–01; 8:45 am]

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Dawn P. Hawkins